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Datasheet for the decision of 5 May 2022

Case Number: T 2680/19 - 3.3.04

Application Number: 08845718.9

Publication Number: 2214699

IPC: A61K38/00, A61K38/47, C07K14/81

Language of the proceedings: EN

Title of invention:
Method, composition, and article of manufacture for providing alpha-1 antitrypsin

Patent Proprietor:
Grifols Therapeutics Inc.

Opponent:
CSL Behring GmbH

Headword:
Alpha-1 antitrypsin for subcutaneous administration/GRIFOLS THERAPEUTICS

Relevant legal provisions:
EPC Art. 123(2)
EPC R. 103(4)(a)

Keyword:
Auxiliary requests 1 to 6 - amendments allowable (no)
Reimbursement of appeal fee - withdrawal of appeal

Decisions cited:
G 0002/10

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Case Number: T 2680/19 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 5 May 2022

Respondent: (Patent Proprietor)	Grifols Therapeutics Inc. 4101 Research Commons 79 TW Alexander Drive Research Triangle Park, NC 27709 (US)
Representative:	Durán Moya, Luis-Alfonso Durán-Corretjer Còrsega, 329 (Paseo de Gracia/Diagonal) 08037 Barcelona (ES)
Appellant: (Opponent)	CSL Behring GmbH Emil-von-Behring-Strasse 76 35041 Marburg (DE)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 17 July 2019 concerning maintenance of the European Patent No. 2214699 in amended form.**

Composition of the Board:

Chair	P. de Heij
Members:	R. Morawetz
	O. Lechner

Summary of Facts and Submissions

I. Appeals were filed by the patent proprietor and by the sole opponent against the opposition division's interlocutory decision finding that European patent No. EP 2 214 699 (hereinafter "the patent"), as amended in the form of auxiliary request 1, and the invention to which it relates meet the requirements of the EPC.

II. The patent was granted on European patent application No. 08 845 718.9, filed as an international patent application published as WO 2009/059082 (hereinafter "application"), entitled "*Method, composition, and article of manufacture for providing alpha-1 antitrypsin*".

III. The opposition proceedings were based, *inter alia*, on the ground for opposition in Article 100(c) EPC. In the decision under appeal, the opposition division considered sets of claims of a main request (patent as granted) and an auxiliary request 1. It held that the subject-matter of claim 1 of the main request extended beyond the content of the application as filed (Articles 100(c) and 123(2) EPC). As for claim 1 of auxiliary request 1, it held that the combination of features characterising the amount of subcutaneously administered alpha-1 antitrypsin met the requirements of Article 123(2) EPC.

Claim 1 of the main request (patent as granted) reads as follows:

"1. Alpha-1 antitrypsin (α1-AT) for use in a method of treating or preventing a disorder or disease associated with α1-AT deficiency in a subject by subcutaneous

administration, wherein the therapeutically or prophylactically effective amount of the subcutaneously administered α1-AT is at least about 120% of an intravenously administered therapeutically or prophylactically effective amount of α1-AT wherein the therapeutically or prophylactically effective amount of α1-AT is sufficient to maintain in the subject a blood α1-AT trough level of at least about 80 mg/dL, wherein the therapeutically or prophylactically effective amount of α1-AT is about 60 mg to about 300 mg of α1-AT per kg of body weight of the subject."

Claim 1 of auxiliary request 1 reads as follows:

"1. Alpha-1 antitrypsin (α1-AT) for use in a method of treating or preventing a disorder or disease associated with α1-AT deficiency in a subject by subcutaneous administration, wherein the therapeutically or prophylactically effective amount of the subcutaneously administered α1-AT is at least about 120% of a therapeutically or prophylactically effective amount of α1-AT based on a dosage regimen comprising intravenously administered α1-AT, wherein the therapeutically or prophylactically effective amount of the subcutaneously administered α1-AT is sufficient to maintain in the subject a blood α1-AT trough level of at least about 80 mg/dL, wherein the therapeutically or prophylactically effective amount of the subcutaneously administered α1-AT is about 60 mg to about 300 mg of α1-AT per kg of body weight of the subject."

IV. In its statement of grounds of appeal, the patent proprietor submitted arguments to the effect that the subject-matter of claim 1 of the claims as granted (main request) did not contain an unallowable extension

of subject-matter (Articles 100(c) and 123(2) EPC).

V. In its statement of grounds of appeal, the opponent (hereinafter "appellant") submitted arguments to the effect that the subject-matter of claim 1 of auxiliary request 1, considered in the decision under appeal, lacked compliance with the requirements of Article 123(2) EPC.

VI. In its reply to the opponent's appeal, the patent proprietor maintained its main request and submitted sets of claims of auxiliary requests 1 to 6. Auxiliary request 1 is identical to auxiliary request 1 held allowable by the opposition division. The patent proprietor presented, *inter alia*, arguments to the effect that the subject-matter of claim 1 of auxiliary request 1 met the requirements of Article 123(2) EPC.

Claim 1 of auxiliary request 2 is identical to claim 1 of auxiliary request 1 (see section III. above).

Claim 1 of auxiliary request 3 differs from claim 1 of auxiliary request 1 in that the expression "*at least about 120%*" has been amended to read "*about 120%*".

Claim 1 of auxiliary request 4 is identical to claim 1 as granted (see section III. above).

Claim 1 of auxiliary request 5 reads as follows:

"1. Alpha-1 antitrypsin (α1-AT) for use in a method of treating or preventing a disorder or disease associated with α1-AT deficiency in a subject by subcutaneous administration of a dose of at least about 120% of the therapeutically or prophylactically effective amount of α1-AT based on a dosing regimen comprising

intravenously administered α1-AT wherein the therapeutically or prophylactically effective amount of α1-AT is sufficient to maintain in the subject a blood α1-AT trough level of at least about 80 mg/dL, wherein the therapeutically or prophylactically effective amount of α1-AT is about 60 mg to about 300 mg of α1-AT per kg of body weight of the subject."

Claim 1 of auxiliary request 6 differs from claim 1 of auxiliary request 5 in that the expression "*at least about 120%*" has been amended to read "*about 120%*".

VII. In its reply to the patent proprietor's appeal, the appellant submitted that none of auxiliary requests 2 to 6 met the requirements of Article 123(2) EPC.

VIII. The board scheduled oral proceedings as per the parties' requests and subsequently issued a communication pursuant to Article 15(1) RPBA. In this communication, the board informed the parties, *inter alia*, that it was inclined to agree with the appellant that the subject-matter of claim 1 of all the claim requests on file related to a combination of features that was not directly and unambiguously derivable from the application as filed.

IX. The patent proprietor provided further arguments in support of there being a basis in the application as filed for the subject-matter of claim 1 of the main request.

X. During the oral proceedings the patent proprietor (hereinafter "the respondent") withdrew its appeal. At the end of the oral proceedings, the Chair announced the board's decision.

XI. The appellant's arguments, as far as relevant to the decision, are summarised below.

Auxiliary request 1

Amendments (Article 123(2) EPC) - claim 1

Claim 1 defined the subcutaneously administered amount of α1-AT on account of three features: (i) a dose adjustment factor of 120% of an intravenously administered amount; (ii) achieving a trough level of at least 80 mg/dL; and (iii) a dose of 60 mg to 300 mg per kg of body weight of the subject.

The application as filed disclosed three different approaches, corresponding to features (i), (ii) and (iii), as alternative, separate solutions for treating α1-AT deficiency, and not as combined features within a single method of α1-AT administration (see page 2, line 25 to page 3, line 4; page 6, line 30 to page 7, line 26; claim 2).

Moreover, as evidenced by the language used in the application (e.g. on page 2, lines 25 and 31; page 3, line 4; page 7, lines 10 and 19), these three different approaches were labelled as relating to separate aspects and separate embodiments. Different aspects had to be considered equivalent to different independent claims and could not be combined. The embodiments, while narrower than the aspects, could not be combined either because the application did not link an embodiment of one aspect to another aspect. Nor did the application provide any technical information for features (ii) and (iii) or any reason for combining those features with feature (i).

The passage on page 6, lines 11 et seq. did not provide any further information beyond defining pharmacokinetic parameters.

The examples provided a rationale for feature (i) but not for combining it with features (ii) and (iii); see e.g. Figure 2. In fact, the examples pointed to different combinations.

The claims as filed did not provide any pointer to the claimed combination of features because they do not mention features (ii) and (iii).

The wrong criterion had been applied in the decision under appeal because being part of the same invention was not the test for compliance with Article 123(2) EPC set out in G 2/10.

The case law relied on by the respondent also required there to be a pointer to the claimed combination of features. Pointers could be statements in the application to the effect that certain features were preferred, advantageous or recited in claims.

However, the application did not state a preference for any embodiment. The concept of "bioavailability" could not provide a pointer to the claimed combination of features (i), (ii) and (iii) because the application did not disclose that any of those features had been optimised for achieving bioavailability.

It might be obvious to combine the three features but there was no pointer towards the combination. Therefore, a method for subcutaneous administration of α1-AT characterised by having all three features (i), (ii) and (iii) was not directly and unambiguously

derivable from the application.

Auxiliary requests 2 to 6 - claim 1

Amendments (Article 123(2) EPC)

The subject-matter of claim 1 of auxiliary requests 2 to 6 included the same combination of features as claim 1 of auxiliary request 1, so the same objection applied.

XII. The respondent's arguments, as far as relevant to the decision, are summarised below.

Auxiliary request 1

Amendments (Article 123(2) EPC) - claim 1

The two approaches disclosed in the application for determining the subcutaneous dose of α1-AT, corresponding to features (i) and (ii) of the claim, dealt with the same invention and were not alternative embodiments. Therefore, there was no undisclosed combination of features in the claim. Although the passages disclosing these features started with "*In one aspect, ...*" (see page 2, line 25 of the application) and "*In another aspect, ...*" (see page 2, line 31 of the application), the skilled person would understand that the trough level and dose range were merely a specification of what the invention also entailed.

The amount of about 60 mg to about 300 mg was disclosed as part of another embodiment of the same invention described on pages 2 and 3 of the application; it was specifically highlighted (see page 7, lines 19 to 26 of the application). It would be an "overly formalistic,

semantic approach" to say that the words "embodiments" and "aspects" constituted a strict separation; there was a reason why this information was provided in one document.

According to the case law of the boards of appeal, the relevant question was whether the skilled person would seriously contemplate combining the features recited in the application, e.g. because of a pointer linking the features together (see also T 171/10).

From the application, the skilled person knew that when changing from intravenous to subcutaneous injection, sufficient bioavailability was the important issue (see page 2, lines 15 to 16 and 20 to 22; page 6, lines 11 et seq.; Examples 1 and 2). Achieving the required bioavailability for a subcutaneous administration of α1-AT to be therapeutically or prophylactically effective served as a pointer to the claimed combination of features. All three definitions of the amount of the subcutaneously administered α1-AT served to ensure sufficient bioavailability of the α1-AT. They were not mutually exclusive alternatives. The skilled person reading the application recognised that these definitions could be used in combination to define a suitable subcutaneous therapy. It was obvious to the skilled person to combine the three features recognised in the application to be necessary for achieving the required bioavailability, because complying with all three features "was of course the best way and hence preferred".

Furthermore, combining embodiments was possible when it was apparent that they related to independent preferred aspects of the invention, which could thus be combined (see also T 1563/13). Reading the application as a

whole, the skilled person would have noted the peculiar use of the terms "aspect" and "embodiment" and understood that an "embodiment" was narrower than what came before and was therefore – inherently – "preferred". Pursuant to T 389/13, it was permitted to take account of both the function (here: ensuring bioavailability) and the interaction of the features that were combined. All three features were clearly the preferred ones (see page 2, lines 29 to 31; page 3, lines 3 to 4 and claim 2; page 7, lines 25 and 26).

In the context of novelty, the boards of appeal had held that it was permissible to combine passages in a document provided that there were no reasons that would prevent the skilled person from doing so (T 332/87 or T 1850/10).

Therefore, combining the three definitions of the amount of the subcutaneously administered α1-AT in claim 1 did not add subject-matter.

Auxiliary requests 2 to 6 - claim 1

Amendments (Article 123(2) EPC)

No arguments were provided as to why the claimed combination of features met the requirements of Article 123(2) EPC.

XIII. As far as relevant to the present decision, the appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent requested that the opponent's appeal be rejected, i.e. that the patent be maintained on the basis of auxiliary request 1, which was submitted with

the reply to the opponent's statement of grounds of appeal and identical to auxiliary request 1 considered allowable in the decision under appeal. It also requested reimbursement of 25% of the appeal fee.

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is admissible.

Auxiliary request 1

Amendments (Article 123(2) EPC) - claim 1

2. The claim, which is identical to claim 1 of auxiliary request 1 considered in the decision under appeal, is for the use of α1-AT in a method of treating α1-AT deficiency in a subject by subcutaneous administration. The effective amount of the subcutaneously administered α1-AT is defined by three features:

(i) it is at least about 120% of a therapeutically or prophylactically effective amount of α1-AT based on a dosage regimen comprising intravenously administered α1-AT;
(ii) it is sufficient to maintain in the subject a blood α1-AT trough level of at least about 80 mg/dL; and
(iii) it is about 60 mg to about 300 mg of α1-AT per kg of body weight of the subject.

3. It is undisputed that the application does not verbatim disclose a method in which the amount of the subcutaneously administered α1-AT is characterised by features (i), (ii) and (iii). The opposition division held that while the three features characterising the

amount of the subcutaneously administered α1-AT were disclosed individually in the application, they could be combined without adding subject-matter because they were all "part of the same invention" (see decision under appeal, Reasons 11.4). On appeal, the appellant maintained that a method of treating α1-AT deficiency in which the amount of α1-AT to be subcutaneously administered was defined by the claimed combination of features (i), (ii) and (iii) was contrary to the requirements of Article 123(2) EPC.

4. It is established case law of the boards of appeal that the standard for assessing compliance with the requirements of Article 123(2) EPC is the standard set out in decision G 2/10 (OJ EPO 2012, 376, Reasons, point 4.3), also known as the "gold standard". Amendments are only permitted within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively and relative to the date of filing, from the whole of the application as filed.

5. It is also well established in the case law of the boards of appeal that the content of an application must not be considered to be a reservoir from which features pertaining to separate embodiments of the application can be combined in order to artificially create a particular embodiment. In the absence of any pointer to that particular combination, this combined selection of features does not, for the person skilled in the art, emerge clearly and unambiguously from the content of the application as filed (see Case Law of the Boards of Appeal, 9th edition, 2019, ("CLBA"), II.E.1.6.1).

6. The application relates to a method for providing to a subject, by a subcutaneous route, a therapeutically or prophylactically effective amount of α1-AT for treating or preventing a disorder or disease associated with α1-AT deficiency (see e.g. page 1, lines 9 to 11; claim 1). In the section relating to the background of the invention, the application states that it is known that α1-AT deficiency can be treated by repeated intravenous administrations of α1-AT, but that this mode of administration can be associated with problems (see page 2, lines 15 to 19). There remained therefore a need "*for a method for providing α1-AT that at least is easy to administer, is suitable for long-term administration, and achieves desirable α1-AT plasma bioavailability levels*" (see page 2, lines 20 to 22).

7. The application then discloses three approaches for defining the amount of subcutaneously administered α1-AT (see page 2, line 25 to page 3, line 4; page 6, line 30 to page 7, line 9; claim 2) as set out below.

7.1 In a first approach, termed "one aspect" (see page 2, line 25 or page 6, line 30 of the application), the amount of α1-AT to be administered subcutaneously is specified as being a therapeutically or prophylactically effective amount. According to "*one embodiment*" of this aspect, the effective amount of α1-AT is specified on the basis of a target blood α1-AT trough threshold level "*sufficient to maintain a blood α1-AT trough level of at least 80 mg/dL*" (see page 2, lines 25 to 30). This embodiment corresponds to feature (ii) of claim 1. Further embodiments of this aspect define different target threshold levels as "*at least about 10 mg/dL, illustratively, about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, and*

200 mg/dL" (see page 7, lines 1 to 3), and in the context of human subjects as "*at least about 50 mg/dL*" or "*at least about 80 mg/dL*" (see page 7, lines 4 to 8).

7.2 In a second approach, termed "*another aspect*" or "*other embodiments*" (see page 2, line 31 or page 7, line 10 of the application), the effective amount of α1-AT to be subcutaneously administered is defined by reference to a dosing regimen comprising intravenous administration of α1-AT to a subject and application of a dose adjustment factor of 120% to the intravenous dose (see application, page 2, line 31 to page 3, line 4; page 7, lines 10 to 16; claim 2). This approach corresponds to feature (i) of claim 1.

7.3 As a third approach, the dose of α1-AT to be subcutaneously administered is directly specified in terms of possible dose ranges as follows: "*In one embodiment, the dose to be subcutaneously administered is at least about 1 mg per kg of body weight of the subject per subcutaneous administration, illustratively, about 1 mg to about 1000 mg, about 10 mg to about 900 mg, about 20 mg to about 800 mg, about 30 mg to about 700 mg, about 40 mg to about 600 mg, about 50 mg to about 500 mg, about 60 mg to about 400 mg, about 70 mg to about 300 mg, about 80 mg to about 250 mg, about 90 mg to about 200 mg, and about 100 mg to about 150 mg per kg of body weight of subject per administration. In another embodiment, the dose is about 60 mg to about 300 mg per kg of body weight of the subject*" (see page 7, lines 19 to 26 of the application). The embodiment termed "*another embodiment*" corresponds to feature (iii) of claim 1.

8. The three features (i), (ii) and (iii) defining the subcutaneously administered amount of α1-AT in claim 1 are disclosed in the application explicitly as distinct "aspects" and separate "embodiments" of alternative methods for providing to a subject, by a subcutaneous route, a therapeutically or prophylactically effective amount of α1-AT; they are not disclosed as combined features within a single α1-AT administration method (see application, page 2, lines 25 and 31; page 6, line 30; page 7, lines 4, 6, 10, 19 and 25).

9. None of the passages of the application disclosing features (i), (ii) and (iii) of claim 1 links an embodiment of one aspect to a different aspect or to an embodiment of a different aspect (see application, page 2, line 25 to page 3, line 4; page 6, line 30 to page 7, line 26).

10. The application furthermore discloses that one factor that may be considered when determining a therapeutically or prophylactically effective amount of α1-AT for subcutaneous administration is the pharmacology of α1-AT. Pharmacokinetic parameters or measures of α1-AT levels in the blood are said to include the area under the curve (AUC), C_{min} (= trough level), and C_{max}, the trough level being the lowest blood level of α1-AT during a fixed dosing period (see page 6, lines 8 to 16). However, the application does not provide any information on how the trough levels, dose adjustment factor and dose ranges generally - or features (i), (ii) and (iii) specifically - interact to achieve a therapeutically or prophylactically effective amount of α1-AT upon subcutaneous administration.

11. In Example 1, the plasma bioavailability of subcutaneously administered α1-AT was determined in

rabbits. A single injection of two subcutaneous (SC) dose levels, 200 mg/kg body weight (SC-1) and 240 mg/kg body weight (SC-2), were examined and compared with a single intravenous (IV) administration of α1-AT (200 mg/kg body weight). The results were summarised as follows: "*The fractional availability (F) derived from the area under concentration curve's (AUC's) of SC-1 (i.e., 100% IV dose) and SC-2 (i.e., 120% of IV dose) group were, respectively, 27% lower (P<0.05) and 8% lower (not statistically significant) compared to the IV group*" (see page 14, lines 22 to 25). Accordingly, Example 1 provides a rationale for feature (i) but not for combining it with features (ii) and (iii).

12. In Example 2, plasma bioavailability after three repeated subcutaneous administrations of α1-AT was examined. Groups of rabbits were dosed on day 0, 2, 4 and 6 at 50mg/kg (SC-3), 60mg/kg (SC-4) and 70mg/kg (SC-5). The fractional availability, determined by comparing the AUC to the single-dose IV group from the experiment described in Example 1, was 0.71 ± 0.03, 0.89 ± 0.04 and 0.91 ±0.07 for SC-3, SC-4 and SC-5, respectively. A trough level of at least 80 mg/dL was not reached in any of the three SC groups (see Figure 2). Accordingly, Example 2 does not provide a rationale for combining features (i), (ii) and (iii) either.

13. While the claims as filed disclose subject-matter corresponding to feature (i) of claim 1 (see claim 2 as filed), they provide no link between that feature and features (ii) and (iii). In fact, subject-matter corresponding to features (ii) and (iii) is not disclosed in the claims as filed.

14. The board concludes from the above analysis (see points 6. to 13.) that the application discloses features (i), (ii) and (iii) as distinct, alternative embodiments of three different methods of providing to a subject, by a subcutaneous route, a therapeutically or prophylactically effective amount of α1-AT, not as features within a single administration method.

The application does not provide any technical information as regards the trough level corresponding to feature (ii), the dose range corresponding to feature (iii) or their interaction with feature (i) in providing to a subject, by a subcutaneous route, a therapeutically or prophylactically effective amount of α1-AT. No other technical information linking features (i), (ii) and (iii) is provided in the application either.

Accordingly, the application provides no incentive or pointer for the skilled person to combine a blood α1-AT trough level of 80 mg/dL and a dose range of about 60 mg to about 300 mg of α1-AT per kg of body weight of the subject with a dose adjustment factor of at least about 120% within a single method of subcutaneous α1-AT administration.

15. The board is not persuaded by the respondent's line of reasoning that claim 1 does not relate to an undisclosed combination of features because the skilled person would immediately understand that the trough level and dose adjustment factor were not alternative embodiments but merely a specification of what "the invention also entails" and the dose range was "part of another embodiment of the same invention".

16. The property of belonging to the same invention does not set the embodiments on which features (i), (ii) and (iii) are based apart from all other embodiments of the invention. Accordingly, being part of the same invention cannot act as a pointer to the claimed combination of features (see point 5. above). For the same reasons, the opposition division's reasoning (see point 3. above) cannot hold either.

17. The respondent's further argument that it was an "overly formalistic, semantic approach" to say that the words "embodiments" and "aspects" constituted a strict separation and that there was a reason why this information was provided in one document - the application - likewise fails. This argument ignores the fact that the content of an application must not be considered to be a reservoir from which features pertaining to separate embodiments of the application can be combined in order to artificially create a particular embodiment (see point 5. above).

18. The respondent furthermore submitted that the required bioavailability for a subcutaneous administration of α1-AT to be therapeutically or prophylactically effective acted as a pointer, meaning that the skilled person, after being told in the application that sufficient bioavailability was important for the subcutaneous therapy (see page 2, lines 20 to 22 of the application), would recognise that the definitions corresponding to features (i), (ii) and (iii) could be used in combination to define a suitable subcutaneous therapy, and that satisfying all three features "was of course the best way and hence preferred".

19. However, as set out above (see points 7. to 8.), the application discloses three alternative approaches for

defining the amount of the subcutaneously administered α1-AT, with the first approach (based on target blood α1-AT trough threshold levels) and the third approach (based on α1-AT dose ranges) encompassing several alternative embodiments. Even if it were accepted that "achieving bioavailability" could serve as a pointer towards combining the three alternative approaches into a single method, the skilled person would require an incentive or pointer to choose the particular combination of embodiments corresponding to features (i), (ii) and (iii) from among all the other possible combinations of embodiments.

20. The respondent's submission in this context that features (i), (ii) and (iii) were disclosed as being preferred and could therefore be combined is not found persuasive.

In the application, the embodiment corresponding to feature (ii) (i.e. blood α1-AT trough level of at least about 80 mg/dL) is disclosed as "one embodiment", and the feature corresponding to feature (iii) (i.e. 60 mg to about 300 mg of α1-AT per kg of body weight) is disclosed as "another embodiment" (see points 7.1 and 7.3). Neither embodiment is stated as being "preferred". Nor does the application disclose that the embodiments corresponding to features (ii) and (iii) are particularly advantageous or optimised in terms of ensuring sufficient bioavailability compared with all the other trough levels and dose ranges disclosed (see also point 10. above).

21. The respondent's further argument that a preference was implied because the skilled person would have understood that an "embodiment" was narrower than an "aspect" cannot succeed because the application

discloses several embodiments for the trough level (see point 7.1) and several embodiments for the dose range (see point 7.3).

Furthermore, if it were accepted that "being narrower" implied a preference, then the application would point to different embodiments; 80 mg/dL is not the narrowest option for the trough level (see point 7.1 above), and 60 mg to about 300 mg of α1-AT per kg of body weight is not the narrowest option for the dose range (see point 7.3 above).

In sum, a preference for features (ii) and (iii), and hence a pointer towards combining them with feature (i) in the context of bioavailability, is not derivable from the application.

22. Lastly, as regards the respondent's reliance on established case law for assessing novelty, the board notes that also when contesting novelty, the content of a document must not be treated as something in the nature of a reservoir from which features pertaining to separate embodiments may permissibly be drawn in order to create artificially a particular embodiment which would destroy novelty, unless the document itself suggests such a combination of features (see CLBA, section I.C.4.2).

23. The board concludes that the subject-matter of claim 1 relates to subject-matter that is not directly and unambiguously derivable from the application as filed (Article 123(2) EPC).

Auxiliary requests 2 to 6

24. The respondent requested that the opponent's appeal be rejected, implying that the patent be maintained on the basis of auxiliary request 1, but did not refer to its lower-ranking claim requests, i.e. auxiliary requests 2 to 6 submitted with the reply to the statement of grounds of appeal. In case the respondent implicitly wished to maintain the lower-ranking claim requests, the board notes the following.

25. Claim 1 of each of auxiliary requests 2 to 6 contains the same combination of features, (i), (ii) and (iii), as claim 1 of the main request (see section VI.). The reasoning set out above for claim 1 of the main request (see points 2. to 23.) therefore applies *mutatis mutandis* to the subject-matter of claim 1 of each of auxiliary requests 2 to 6. This was not disputed by the respondent. Consequently, the subject-matter of claim 1 of auxiliary requests 2 to 6 does not meet the requirements of Article 123(2) EPC.

Reimbursement of the appeal fee

26. As stated under section X. above, the patent proprietor withdrew its appeal before the decision was announced at oral proceedings. As a consequence, the appeal fee paid by the patent proprietor is to be reimbursed at 25% in accordance with Rule 103(4)(a) EPC. A separate order for the reimbursement has been issued.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

I. Aperribay P. de Heij

Decision electronically authenticated